b) screening the library to identify an optimized recombinant polynucleotide that has, or encodes a polypeptide that has, a modulatory effect on an immune response induced by a vector;

wherein the optimized recombinant polynucleotide or the polypeptide encoded by the recombinant polynucleotide exhibits an enhanced ability to modulate an immune response compared to a polynucleotide from which the library was created;

wherein said optimized modulatory effect on an immune response is induced by a genetic vaccine vector, wherein the optimized recombinant polynucleotide encodes a co-stimulator selected from B7-1 (CD80) or B7-2 (CD86) and the screening step involves selecting variants with altered activity through CD28 or CTLA-4, and whereby optimization is achieved by recursive sequence recombination.

48.   (New) A method for obtaining an immunomodulatory polynucleotide that has an optimized modulatory effect on an immune response as compared to the response prior to optimization, or encodes a polypeptide that has an optimized modulatory effect on an immune response as compared to the response prior to optimization, the method comprising:

a) creating a library of recombinant polynucleotides; and

b) screening the library to identify an optimized recombinant polynucleotide that has, or encodes a polypeptide that has, a modulatory effect on an immune response induced by a vector;

wherein the optimized recombinant polynucleotide or the polypeptide encoded by the recombinant polynucleotide exhibits an enhanced ability to modulate an immune response compared to a polynucleotide from which the library was created;

wherein said optimized modulatory effect on an immune response is induced by a genetic vaccine vector, wherein the optimized recombinant polynucleotide encodes a co-stimulator selected from a B7-1 (CD80) variant or a B7-2 (CD86) variant and the screening step involves selecting variants with altered activity through CD28 or CTLA-4, and whereby optimization is achieved by recursive sequence recombination.